

Appl. No. : 10/564,804  
Filed : January 13, 2006

#### REMARKS

In response to the Notice of Non-Compliant Amendment dated August 24, 2007, Applicants filed a Supplemental Response to the Restriction Requirement on August 24, 2007 in which the inadvertently omitted text of the claims directed to the non-elected Groups II and III, Claims 11-13, was presented. A copy of the Supplemental Response to the Restriction Requirement filed on August 24, 2007 is enclosed herewith. Applicants apologize for any inconvenience this may cause the Examiner and respectfully request prompt examination on the merits of Claims 1-10 and 14.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 29 August 2007

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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Thakashinamoorthy et al.  
Appl. No. : 10/564,804  
Filed : January 13, 2006  
For : PROCESS FOR THE  
MANUFACTURE OF  
ISRADIPINE  
Examiner : P.L. Morris  
Group Art Unit : 1625

CERTIFICATE OF EFS WEB  
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I hereby certify that this correspondence, and any other attachment noted on the automated Acknowledgement Receipt, is being transmitted from within the Pacific Time zone to the Commissioner for Patents via the EFS Web server on:

24 August 2007

(Date)

Joseph J. Mallon  
Joseph J. Mallon, Reg. No. 39,287

SUPPLEMENTAL RESPONSE TO RESTRICTION REQUIREMENT

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In addition to the Response to the Restriction Requirement filed August 20, 2007, please consider the following additional remarks.

**Amendments to the Claims** are reflected in the listing of claims which begins on page 2 of this paper.

**Remarks** begin on page 5 of this paper.

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### AMENDMENTS TO THE CLAIMS

Please amend Claim 1 and add new Claim 14 as shown below.

1. (CURRENTLY AMENDED) An improved method for the manufacture of 4-(4-Benzofuranzanyl)-1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylic acid methyl 1-methylethyl ester comprising the steps of:

(i) reacting 2,1,3-benzoxadiazole-4-carboxaldehyde with methyl acetoacetate in the presence of acetic acid and piperidine in diisopropyl ether to obtain 2-acetyl-3-benzofurazan-4-yl-acrylic acid methyl ester;

(ii) isolating and purifying 2-acetyl-3-benzofuran-4-yl-acrylic acid methyl ester to obtain purified 2-acetyl-3-benzofuran-4-yl-acrylic acid methyl ester by recrystallization from a solvent;

(iii) reacting 2-acetyl-3-benzofuran-4-yl-acrylic acid methyl ester with isopropyl- $\beta$ -aminoacrylate in ethanol to obtain 4-(4-Benzofuranzanyl)-1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylic acid methyl 1-methylethyl ester.

2. (ORIGINAL) An improved process as claimed in claim 1 wherein step (iii) is carried out at 25 to 40°C.

3. (ORIGINAL) An improved process as claimed in claim 2 wherein step (iii) is carried out at 25 to 35°C.

4. (ORIGINAL) An improved process as claimed in claim 1 wherein about 0.9 to 1.1 mol of methyl acetoacetate is used for every 1.0 mole of 2,1,3-benzoxadiazole-4-carboxaldehyde.

5. (ORIGINAL) An improved process as claimed in claim 4 wherein about 0.95 to 1.0 mol of methyl acetoacetate is used for every 1.0 mol of 2,1,3-benzoxadiazole-4-carboxaldehyde.

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6. (ORIGINAL) An improved process as claimed as claim 1 wherein acetic acid and piperidine are used in catalytic amount.

7. (ORIGINAL) An improved process as claimed in claim 6 wherein about 0.25 to 3.0 mol of acetic acid and about 0.8 to 0.06 mol of piperidine is used for every 1 mol of 2,1,3-benzoxadiazole-4-carboxaldehyde.

8. (ORIGINAL) An improved process as claimed in claim 1 wherein the 2-acetyl-3-benzofuran-4-yl-acrylic acid methyl ester obtained in step (ii) is crystallized from diisopropyl ether to obtain pure 2-acetyl-3-benzofuran-4-yl-acrylic acid methyl ester.

9. (ORIGINAL) An improved process as claimed in claim 1 wherein about 0.9 to 1.05 mol of isopropyl- $\beta$ -aminocrotonate is used for every 1 mol of 2-acetyl-3-benzofuran-4-yl-acrylic acid methyl ester.

10. (ORIGINAL) An improved process as claimed in claim 9 wherein about 0.9 to 1.00 mol of isopropyl- $\beta$ -aminocrotonate is used for every 1 mol of 2-acetyl-3-benzofuran-4-yl-acrylic acid methyl ester.

11. (WITHDRAWN) A process for purification of 2-acetyl-3-benzofuran-4-yl-acrylic acid methyl ester by recrystallization from a solvent.

12. (WITHDRAWN) A process according to claim 11 wherein the preferred solvents are chosen from ethers, alcohols and mixtures thereof.

13. (WITHDRAWN) A process according to claim 11, wherein the 2-acetyl-3-benzofuran-4-yl-acrylic acid methyl ester thereafter is converted to isradipine.

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14. (NEW) An improved process as claimed in claim 1 wherein the solvent is selected from the group consisting of an ether, an alcohol and a mixture thereof.

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#### REMARKS

In the Response to the Restriction Requirement filed August 20, 2007, Applicants inadvertently omitted the text of the claims directed to the non-elected Groups II and III, Claims 11-13. As shown herein, the text of Claims 11-13 has been added. Applicants apologize for any inconvenience this may cause the Examiner and respectfully request prompt examination on the merits of Claims 1-10 and 14.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 24 August 2007

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